

BRIEF COMMUNICATION

Ten novel HLA-DRB1 alleles and one novel DRB3 alleleA. M. Lazaro¹, N. K. Steiner¹, M. E. Moraes², J. R. Moraes², J. Ng¹, R. J. Hartzman³ & C. K. Hurley¹¹ Departments of Oncology and Pediatrics, Georgetown University Medical Center, Washington, DC, USA² Laboratorio de Imunogenetica Instituto Nacional Do Cancer, Rio de Janeiro, Brazil³ C.W. Bill Young Marrow Donor Program, Naval Medical Research Center, Kensington, MD, USA**Key words**

DNA sequencing; HLA-DR

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Received 20 May 2005, revised and accepted
for publication 31 May 2005

doi: 10.1111/j.1399-0039.2005.00459.x

Abstract

Ten novel HLA-DRB1 and one DRB3 alleles are described. Eight of the variants are single-nucleotide substitutions, four resulting in an amino acid change (DRB1*1145, *1148, *0828 and *1514) and four with silent substitutions (DRB1*040504, *130103, *160502 and DRB3*020204). Two alleles differ by two nucleotide changes altering one (DRB1*1447 and *1361) amino acid and one allele alters three nucleotides and two amino acids.

This article describes 10 novel HLA-DRB1 and one DRB3 alleles identified during low-resolution DNA-based sequence-specific probe typing. Exon 2 was amplified by the polymerase chain reaction using intron primers (I1-RB6, I2-RB7, I1-RB14, I2-RB28, I1-RB40, I2RB39, I1-RB9, I1-RB3, I1-RB32 and I2-RB36) described by Blasczyk and colleagues (1). Sequencing of the second exon was performed using sense primers (I1-RBSeq1 and -3) (1) and an antisense primer I1-RBSeq4 (5'-cagtcacagggactcag-3') in order to sequence both DNA strands.

The cells evaluated in this study are listed in Table 1. Table 2 compares the novel sequences to the sequences of the most homologous alleles.

Acknowledgments

This research was supported by funding from the Office of Naval Research N00014-90-1-0795 and 00014-00-1-0898 to the C.W. Bill Young Marrow Donor Recruitment and Research Program. The views expressed in this article are those of the authors and do not reflect the official policy of the Department of the Navy, the Department of Defense or the U.S. Government.

Report Documentation Page			Form Approved OMB No. 0704-0188		
Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.					
1. REPORT DATE 2005		2. REPORT TYPE N/A		3. DATES COVERED -	
4. TITLE AND SUBTITLE Ten novel HLA-DRB1 alleles and one novel DRB3 allele				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S)				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Departments of Oncology and Pediatrics, Georgetown University Medical Center, Washington, DC				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Naval Medical Research Center 503 Robert Grant Avenue Silver Spring, MD 20910-7500				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT SAR	18. NUMBER OF PAGES 3	19a. NAME OF RESPONSIBLE PERSON
a. REPORT unclassified	b. ABSTRACT unclassified	c. THIS PAGE unclassified			

Table 1 Cells and their HLA alleles

Cell	HLA-A ^a	HLA-B ^a	HLA-DR ^b	GenBank Accession No. ^c
GN00419	A*02, A*23	B*35, B*4501	DRB1*040504 , DRB1*1104, DRB3*02	AY094139
MMMBR	A*0201, A*06802	B*4403, B*27	DRB1*0101, DRB1*0828^d	AY504815
NT00504	A*02, A*03	B*07, B*3905	DRB1*04, DRB1*1145	AY429723
NT00507	A*02, A*68	B*49, B*51	DRB1*1148 , DRB1*040501, DRB3*02	AY429728
GN00424	A*03, A*3402	B*35, B*4402	DRB1*130103 , DRB1*0101	AY178184
BY00049	Not tested	Not tested	DRB1*1361 , DRB1*1302	AY339247
BY00050	A*02, A*31	B*35, B*51	DRB1*1447 , DRB1*0407	AY267905
BY00051	A*02	B*1530, B*4901	DRB1*0101, DRB1*1448	AY267906
BY00052	A*11, A*24	B*15, B*35	DRB1*1501, DRB1*1514	AY429729
NT00502	A*11, A*24	B*35, B*51	DRB1*04031, DRB1*160502 , DRB5*0202,	AY428805
GN00418	A2, A31	B51, B60	DRB1*1405, DRB1*09012, DRB3*020404 , DRB4*01 ^d	AY094138

^aHLA-A and -B were assigned primarily by probe-based typing.

^bNovel allele is in bold type. The names have been officially assigned by the WHO Nomenclature Committee.

^cAccession number of novel allele.

^dDQ assignments – MMMBR: DQB1*0501, *0301; GN00418: DQB1*05031, DQB1*0303.

Table 2 Description of novel sequences

Novel allele ^a	Allele most homologous ^b	Difference (nucleotides)	Codon changes ^{c,d}	Amino acid changes	Polymorphisms found at the codon position changed	
					Within the group ^d	Within all DRB ^d
DRB1*040504	DRB1*040501	One	90-ACA to ACG	Silent	ACA (T) 49 ACG (T) 2	ACA (T) 379 ACG (T) 28 CAG (Q) 2 TCC (S) 1 CAC (H) 1 GTG (V) 1
DRB1*0828	DRB1*0804	One	47-TAC to TTC	Y to F	TAC (Y) 33 TTC (F) 2	TAC (Y) 285 TTC (F) 181 GCG (A) 2 TCC (S) 1 TCA (S) 1 TAT (Y) 1 CTC (L) 1
DRB1*1145	DRB1*1123	One	67-TTC to ATC	F to I	TTC (F) 43 ATC (I) 11 CTC (L) 10	CTC (L) 218 ATC (I) 132 TTC (F) 118 GAG (E) 2 CCA (P) 1 CTG (L) 1
DRB1*1148	DRB1*1102	One	47-TTC to TAC	F to Y	TTC (F) 58 TAC (Y) 6	TAC (Y) 214 TTC (F) 174 TAT (Y) 1 CTC (L) 1
DRB1*130103	DRB1*130101	One	78-TAC to TAT	Silent	TAC (Y) 71 TAT (Y) 1	TAC (Y) 330 TAT (Y) 46 GTG (V) 12 CAC (H) 1 TGC (I) 1

Table 2 Continued

DRB1*1361	DRB1*130101	Two	77-ACC to AAT	T to N	ACC (T) 70 AAC (N) 1 AAT (N) 1	ACC (T) 382 AAT (N) 52 AAC (N) 31 TGC (C) 2 GAC (D) 2 GCC (A) 1 TAC (Y) 1 TCG (S) 1
DRB1*1447	DRB1*1402	Two	77-ACC to AAT	T to N	ACC (T) 50 AAT (N) 2 GCC (A) 1	Same as above
DRB1*1448	DRB1*1402	Three	57-GAT to GTC 60-TAC to TCC	D to V Y to S	57 GAT (D) 35 GCT (A) 16 AGC (S) 1 GTC (V) 1 60 TAC (Y) 34 CAC (H) 18 TCC (S) 1	57 V and 60S Observed at some DRB1*07, 09, 12 and *1354
DRB1*1514	DRB1*150201	One	20-GGG to GCG	G to A	GGG (G) 21 GCG (A) 1	GGG (G) 469 GCG (A) 1 CCT (P) 1
DRB1*160502	DRB1*160501	One	69-GAA to GAG	Silent	GAA (E) 9 GAG (E) 1	GAG (E) 248 GAA (E) 218 AAG (K) 2 GGC (G) 1 CAG (Q) 1 CCT (P) 1 GGA (G) 1
DRB3*020204	DRB3*02020	One	58-GCC to GCG	Silent	GCC (A) 20 GCG (A) 2 GAG (E) 1	GCC (A) 298 GAG (E) 72 GCT (A) 66 GCG (A) 27 GCA (A) 3 TAC (Y) 2 TCC (S) 1 GGC (G) 1 ACC (T) 1 CCT (P) 1

^aThe names have been officially assigned by the WHO Nomenclature Committee (2–4).

^bMost homologous sequence obtained from IMGT/HLA Sequence Database (5).

^cFrom first codon of the mature protein. Most homologous allele to novel allele.

^dNew codon is bolded.

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